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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,119	10/04/2004	Linda Dichl	470-045183	4799

7590 09/10/2007

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
09/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,119	DIEHL ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-26* is/are pending in the application.

4a) Of the above claim(s) *26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 13-26 are pending.

Claims 1-12 have been canceled.

2. Applicant's election with traverse of the species (A) treating a tumor in the Election With Traverse, filed 06/08/2007, is acknowledged.

The traversal is on the ground(s) that despite the preamble of the claims, the claims are not directed to treating two separate medical indications.

One of ordinary skill in the art at the time the invention as made would have readily recognized treatments for infectious agents and tumor were clearly distinct therapeutic endpoints. Tumors and infectious agents do not share common structure, function, or source. Further, it is noted that tumors and infectious agents do not do not share a substantial structural feature essential to a common utility do not have common structure to a common utility.

With respect to applicant's assertions that coextensive searching would not present any undue burden, tumors and infectious agents do not share a common structure, function, or source, which results in non-coextensive searching. In turn, they are deemed patentably distinct

Further, applicant's arguments are not found persuasive because with respect to distinctness because as the following of record indicated in the previous Office Action, mailed 04/06/2007.

Applicant's arguments have not been found persuasive.

The requirement is still deemed proper and is therefore made FINAL.

Claims 13-25 are under consideration as they read on the elected invention of species (A) tumor (and not infectious agent) in the instant application.

Claim 26 have been withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to a nonelected species (B) infectious agent.

3. Priority Issues.

The filing date of the instant claims is deemed to be the filing date of PCT/NL03/00254, filed 04/04/2003.

Priority applications USSN 010/115,620, filed 04/04/2002 and USSN 09/316,935, filed 05/22/1999 does not support all of the current claim limitations of the instant application.

If applicant desires priority prior to 04/04/2003, applicant is invited to point out and provide documentary support for the priority of the instant claims.
Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. 112, first paragraph.

A) The recitation of "for induction of systemic T cell immunity against an antigen of the tumor or infectious agent" (versus activating CTLs) appears to receive a priority date back to PCT/NL03/00254, filed 04/04/2003; but not to priority applications USSN 010/115,620, filed 04/04/2002 and USSN 09/316,935, filed 05/22/1999.

B) The recitation of "wherein the treatment does not comprise immunization with an antigen of the tumor or infectious agent" appears to receive a priority date back to the PCT/NL03/00254, filed 04/04/2003; but not to priority applications USSN 010/115,620, filed 04/04/2002 and USSN 09/316,935, filed 05/22/1999.

C) The recitation of "infectious agent" appears to receive a priority date back to PCT/NL03/00254, filed 04/04/2003; but not to priority applications USSN 010/115,620, filed 04/04/2002 and USSN 09/316,935, filed 05/22/1999.

While USSN 010/115,620, filed 04/04/2002, appears to provide written support for "infectious virus", USSN 010/115,620 does not provide for the written support for the broader recitation of "infectious agent" of the instant application.

D) The recitation of "agonistic anti-CD40 antibody" appears to receive a priority back to priority application USSN 010/115,620, filed 04/04/2002; but not to USSN 09/316,935, filed 05/22/1999.

E) The recitation of "tumor-specific antigen" appears to receive a priority date back to PCT/NL03/00254, filed 04/04/2003; but not to priority applications USSN 010/115,620, filed 04/04/2002 and USSN 09/316,935, filed 05/22/1999.

F) The recitation of "intra-tumoral" (versus "directly to the tumor") appears to receive a priority date back to PCT/NL03/00254, filed 04/04/2003; but not to priority applications USSN 010/115,620, filed 04/04/2002 and USSN 09/316,935, filed 05/22/1999.

Given the number of continuation-in-part applications, applicant is invited to clarify the support under 35 USC 112, first paragraph, for the priority of the instant claims in the lineage of priority documents for establishing the record for clarity.

A claim as a whole has only one effective filing date.
See Studiengelsellschaft Kahle m.b.H. v. Shell Oil Co. 42 USPQ2d 1674, 1677 (Fed. Cir 1997).

Again, if applicant desires priority prior to dates indicated above or back to the asserted priority dates for the instant claims; again, applicant is invited to point out and provide documentary support for the priority of the instant claims.

In addition, applicant is invited to consider reciting "limitations" clearly supported by the earliest priority document(s) upon which applicant wants to rely, rather than reciting "limitations" that may be similar but not the same as clearly provided by the written description of the instant and priority documents.

4. If applicant desires priority under 35 U.S.C. § 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

See United States Patent and Trademark Office OG Notices: 1268 OG 89 (18 March 2003).

Applicant should amend the first page of the specification to indicate the status and relationship of the priority documents.

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ® or ™ symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required.

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

7. Claims 18 and 20 are objected to in that $(Fab)_2$ should be $F(ab')_2$ as the proper designation of such antibody fragments.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

8. Claims 13-17, 19-20, 22-23 and 25 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 13-17, 19-20, 22-23 and 25 are indefinite in the recitation of "or a fragment thereof", because the metes and bounds of the claimed antibody fragments are ill-defined and ambiguous.

Although it appears that applicant intends for the "fragment thereof" to be limited to CD40-specific specific antigen binding fragments, it is noted that the Fc component of antibodies / immunoglobulins comprise a number of antibody- / immunoglobulin-related functions, which are distinct from the antigen specificity of the claimed invention.

Applicant is invited to amend the claims to recite "antigen binding fragments" to clarify applicant's intent of the appropriate CD40-specific antigen binding fragments of the claimed methods.

In addition, applicant is invited to consider the issues raised concerning antibody fragments in the rejection under 35 USC 112, first paragraph below.

B) Claims 17 and 20 contain the trademark or trade name "DEIMMUNIZED". Where a trademark or trade name is used in a claims as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 USC 112, second paragraph, See Ex parte Simpson, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark or the trade name " " is used to identify or describe a type of antibody, and accordingly, the identification or the description is indefinite. The relationship between a trademark or tradename and the product it identifies may be uncertain and arbitrary. The formula or characteristics of the product may change from time to time and yet it may continue to be sold under the same trademark or tradename.

C) Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

9. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 13-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite "CD40 receptor".

The recitation of "CD40 receptors" does not meet the written description provision of 35 USC 112, first paragraph. There is insufficient guidance and direction as to the written description of "CD40 receptor", as broadly encompassed by the claimed invention.

While the instant specification does disclose the CD40L (i.,e., CD40 ligand) as the member of the CD40:CD40L pair in immune responses and immunoregulation, the instant application has not provided a sufficient description showing possession of the necessary functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus of "CD40 receptors", broadly encompassed by the claimed invention.

Further, the Court has interpreted 35 U.S.C. §112, first paragraph, to require the patent specification to "describe the claimed invention so that one skilled in the art can recognize what is claimed. Enzo Biochem, Inc. v. Gen-Probe Inc, 63 USPQ2d 1609 and 1618 (Fed. Cir. 2002). In evaluating whether a patentee has fulfilled this requirement, our standard is that the patent's "disclosure must allow one skilled in the art 'to visualize or recognize the identity of' the subject matter purportedly described." Id. (quoting Regents of Univ. of Cal. v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed Cir. 1997)).

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483.

Appellant has been reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Appellants have been directed to Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday January 2001.

Therefore, there is insufficient written description for "CD40 receptors" other than the known CD40L (i.e. CD40 ligand) as known at the time the invention was made and as disclosed in the specification as filed under the written description provision of 35 USC 112, first paragraph.

Applicant is invited to limit the recitation of "CD40 receptor" to CD40L or CD40 ligand in order to obviate this rejection.

11. Claims 18, 21 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the agonistic antigen binding fragments that can bind CD40 and stimulate the CD40 receptor (i.e., CD40 ligand) as set forth in the instant claims and disclosed in the specification as filed, does not reasonably provide enablement for

"V_H, V_L, and Fd fragments" broadly encompassed by the claimed invention.

It has been well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the parent immunoglobulin. All of the heavy and light chain CDRs should be in their proper order and in the context of framework sequences which maintain their required conformation in order to provide a binding molecule having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites.

With respect to antigen-binding fragments, "V_H, V_L, and Fd fragments" do not bind antigen on their own and would not have been predicted to provide the appropriate CD40 binding specificity and CD40 receptor (i.e., CD40 ligand) stimulatory activity as recited by the claimed invention.

Further, it is noted that the instant specification is (and priority documents are) consistent with the use of "V_H, V_L, and Fd fragments" to construct whole human antibodies by applying techniques similar to those for producing chimeric antibodies (see page 13, paragraph 3 of the instant specification), but not as the agonistic antigen binding fragments as the enabled antigen binding fragments required by the claimed methods.

Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the instant disclosure alone. One of skill in the art would neither expect nor predict the appropriate functioning of the claimed "V_H, V_L, and Fd fragments" "to treat a tumor in a subject with an effective amount of agonistic anti-CD40 antibodies or antigen-binding fragments thereof" as broadly as is claimed. Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

Applicant is invited to amend the claims to limit the antigen binding fragments that can provide the appropriate binding and functional attributes required of the instant methods in order to obviate this rejection.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and Was published under Article 21(2) of such treaty in the English language.

13. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 13-25 are rejected under 35 U.S.C. § 102(b) as being anticipated Melief et al. (WO 99/61065) (1449) (see entire document).

Melief et al. teach methods of using dendritic cell activating anti-CD40 antibodies, including chimeric, DEIMMUNISED, humanized and human antibodies, including antigen-binding fragments encompassed by the claimed invention (e.g., see pages 4 and 9-12 and Claims) for the treatment of cancer (e.g., see Summary of the Invention on pages 4-5 and Claims). The Background of the Invention and Summary of the Invention teach the use of such anti-CD40 antibodies to activate dendritic cells and CTLs to act against tumor cells and cancer. Also, Melief et al. teach administration via injection, oral administration or directly to the tumor (e.g., see page 12, paragraph 2 and Claims, including Claim 7).

Melief et al. teach the stimulation via CD40:CD40L, wherein the CD40L was the known receptor for CD40 at the time the invention was made (e.g., see Background of the Invention and Summary of the Invention).

Given the teaching that CD40 ligation can provide an already protective tumor-specific vaccine with the capacity to induce therapeutic CTL immunity in tumor bearing individuals (e.g., see page 5, paragraph 2);

the prior art teaches the induction of T cell immunity to tumor specific antigen wherein the treatment does not comprise immunization with an antigen of the tumor,

since the individual has already been treated with a tumor specific antigen vaccine and the treatment does not require further immunization with the tumor specific antigen.

Although the reference is silent about the induction of "systemic T cell immunity against an antigen of the tumor", "agonistic anti-CD40 antibodies", "wherein the treatment does not comprise immunization with an antigen of the tumor", "intra-tumoral" per se,

it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). "{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable". In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991).

Also, see M.P.E.P. 2145.

On this record, it is reasonable to conclude that the same patient is being administered the same active agent by the same mode of administration in the same amount in both the instant claims and the prior art reference. The fact that applicant may have discovered yet another beneficial effect from the method set forth in the prior art does not mean that they are entitled to receive a patent on that method.

15. Claims 13-25 are rejected under 35 U.S.C. § 102(b) as being anticipated Siegall et al. (US 2004/0235074 A1) (see entire document).

Siegall et al. teach methods of using agonistic anti-CD40 antibodies, which enhance CD40L-mediated interactions, including chimeric and humanized, including antigen-binding fragments encompassed by the claimed invention (e.g., see Detailed Description of the Invention and Examples, including Section 5.6 mAb S2C6 Antibody Derivatives in paragraphs [0081] – [0091]) in order to augment immune responses or the immune system for the treatment of cancer (e.g., see Background of the Invention, Summary of the Invention and Section 5.9 Therapeutic Uses, Section 5.9.1 Effective Dose and Section 5.9.2 Formulations on pages 12-14 and Claims). Here in Section 5.9.2 Formulations, modes of administration via injection and oral administration.

Siegall et al. teach that CD40:CD40L interactions are involved in immune responses and interactions, including dendritic cells (e.g., see Section 2.1 CD40 and CD40 Ligand on page 1)

It is noted that the claims required that "the treatment does not comprise immunization with an antigen of the tumor".

Siegall also teach the Therapeutic Uses of said antibodies for the treatment or prevention of malignancies (including but not limited to carcinoma and hematologic malignancies), wherein the malignant cells express CD40 or need not express CD40, including its use to increase the immune response of an immunosuppressed individual, such as a person suffering from malignancy via the promoting the proliferation and/or differentiation of CD40-bearing cells as a means of directly treating malignancy or as an adjunct to chemotherapy (e.g., see Therapeutic Uses on pages 12-13).

Although the reference does not teach tumor-specific antigens per se, given the Malignancies set forth in Table 1 on pages 12-13, tumor-specific antigens would be inherent to the described tumors.

Although the reference is silent about the induction of "systemic T cell immunity against an antigen of the tumor", "wherein the treatment does not comprise immunization with an antigen of the tumor", "tumor-specific antigen" per se,

it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). "{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable". In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991).

Also, see M.P.E.P. 2145.

On this record, it is reasonable to conclude that the same patient is being administered the same active agent by the same mode of administration in the same amount in both the instant claims and the prior art reference. The fact that applicant may have discovered yet another beneficial effect from the method set forth in the prior art does not mean that they are entitled to receive a patent on that method.

16. Claims 13-25 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Siegall et al. (US 2004/0235074 A1) in view of Melief et al. (WO 99/61065) (1449).

Siegall et al. teach methods of using agonistic anti-CD40 antibodies, which enhance CD40L-mediated interactions, including chimeric and humanized, including antigen-binding fragments encompassed by the claimed invention (e.g., see Detailed Description of the Invention and Examples, including Section 5.6 mAb S2C6 Antibody Derivatives in paragraphs [0081] – [0091]) in order to augment immune responses or the immune system for the treatment of cancer (e.g., see Background of the Invention, Summary of the Invention and Section 5.9 Therapeutic Uses, Section 5.9.1 Effective Dose and Section 5.9.2 Formulations on pages 12-14 and Claims). Here in Section 5.9.2 Formulations, modes of administration via injection and oral administration.

Siegall et al. teach that CD40:CD40L interactions are involved in immune responses and interactions, including dendritic cells (e.g., see Section 2.1 CD40 and CD40 Ligand on page 1)

It is noted that the claims required that "the treatment does not comprise immunization with an antigen of the tumor".

Siegall also teach the Therapeutic Uses of said antibodies for the treatment or prevention of malignancies (including but not limited to carcinoma and hematologic malignancies), wherein the malignant cells express CD40 or need not express CD40, including its use to increase the immune response of an immunosuppressed individual, such as a person suffering from malignancy via the promoting the proliferation and/or differentiation of CD40-bearing cells as a means of directly treating malignancy or as an adjunct to chemotherapy (e.g., see Therapeutic Uses on pages 12-13).

Although the reference does not teach tumor-specific antigens per se, given the Malignancies set forth in Table 1 on pages 12-13, tumor-specific antigens would be inherent to the described tumors.

In addition, Melief et al. teach that CD40 ligation can provide an already protective tumor-specific vaccine with the capacity to induce therapeutic CTL immunity in tumor bearing individuals (e.g., see page 5, paragraph 2);
the prior art teaches the induction of T cell immunity to tumor specific antigen wherein the treatment does not comprise immunization with an antigen of the tumor,
since the individual has already been treated with a tumor specific antigen vaccine and the treatment does not require further immunization with the tumor specific antigen. the treatment for tumor specific antigens,

Siegall et al. does not teach the known applicability of using DEIMMUNISED and human antibodies as therapeutic antibodies at the time the invention was made.

Melief et al. teach methods of using dendritic cell activating anti-CD40 antibodies, including chimeric, DEIMMUNISED, humanized and human antibodies, including antigen-binding fragments encompassed by the claimed invention (e.g., see pages 4 and 9-12 and Claims) for the treatment of cancer (e.g., see Summary of the Invention on pages 4-5 and Claims). The Background of the Invention and Summary of the Invention teach the use of such anti-CD40 antibodies to activate dendritic cells and CTLs to act against tumor cells and cancer.

Although Siegall et al. does not teach administering the anti-CD40 antibodies intra-tumorally, Melief et al. teach administration directly to the tumor in addition to the known and conventional modes of administration via injection and oral administration or (e.g., see page 12, paragraph 2 and Claims, including Claim 7 of Melief et al.).

Melief et al. teach the stimulation via CD40:CD40L, wherein the CD40L was the known receptor for CD40 at the time the invention was made (e.g., see Background of the Invention and Summary of the Invention).

Given the teaching that CD40 ligation can provide an already protective tumor-specific vaccine with the capacity to induce therapeutic CTL immunity in tumor bearing individuals (e.g., see page 5, paragraph 2);

the prior art teaches the induction of T cell immunity to tumor specific antigen wherein the treatment does not comprise immunization with an antigen of the tumor,

since the individual has already been treated with a tumor specific antigen vaccine and the treatment does not require further immunization with the tumor specific antigen.

Also, it is noted that methods of administration encompass a result effective variable. It is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also Merck & Co. v. Biocraft Labs. Inc., 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious). As the claimed methods of administration were known to the ordinary artisan, it would have been obvious to optimize both the mode of administration as well as dosage amounts.

Depending on the needs of the patient and the nature of the therapeutic endpoint, one of ordinary skill in the art at the time the invention was made would have been motivated to provide antagonistic antibodies via multiple modes of administration, including the intravenous, subcutaneous and intramuscular routes of administration as known and practiced at the time the invention was made.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

17. It is noted that the co-inventors have a number of copending applications drawn to methods of treating tumors (and the non-elected species of 'infectous agents") with the same agonistic anti-CD40 antibodies.

Further, it is noted that the copending applications differ in inventorship.

Applicant is invited to clarify which applications should be subject to rejections under the judicially created doctrine of obviousness-type double patenting.

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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September 4, 2007